Department of Veterans Affairs
Veterans Health Administration
Washington DC 20420

Replaces VHA Directive 2000-038; replaced by VHA Directive 2002-044

VHA DIRECTIVE 2001-053

August 28, 2001

INFLUENZA VACCINE – RECOMMENDATIONS FOR 2001-2002

1. PURPOSE: This Veterans Health Administration (VHA) Directive provides guidance on the use of the influenza vaccine for 2001-2002.

2. BACKGROUND

a. For several years the Department of Veterans Affairs (VA) has provided the influenza vaccine to high-risk patients and to employees. Information is provided on vaccine composition, usage (including high-risk groups), contraindications, side effects and adverse reactions, dosage, and related preventive strategies (see Att. A). The program will continue to receive increased emphasis as a part of the VA Preventive Medicine Program, and will be assessed based on the number of doses dispensed.

b. The trivalent influenza vaccine prepared for the 2001-2002 season will include A/Moscow/10/99 (H3N2)-like, A/New Caledonia/20/99 (H1N1)-like, and B/Sichuan/379/99-like antigens. For the A/Moscow/10/99 (H3N2)-like antigen, manufacturers will use the antigenically equivalent A/Panama/2007/99 (H3N2) virus; and for the B/Sichuan/379/99-like antigen, they will use one of the antigenically equivalent viruses B/Johannesburg/5/99, B/Victoria/504/2000, or B/Guangdong/120/2000. These viruses are used because of their growth properties and because they are representative of currently circulating A (H3N2) and B viruses.

c. Manufacturer projections of vaccine distribution for the 2001-02 influenza season suggest that 49.8 million doses will be available for delivery by the end of October 2001; this is approximately 26 million fewer doses of influenza vaccine than were available by the end of October 1999 (75.8 million doses). Manufacturers also project distribution of 27.3 million doses in November and December, bringing the cumulative projected total to 77.1 million doses, which is greater than in 2000 (70.4) and comparable with 1999 (76.8). The numbers for 1999 and 2000 represent aggregate estimated monthly distribution of the influenza vaccine for each of the years represented based on manufacturers' reports. The numbers for 2001 are projections and should be used only as a guide that represents the manufacturers' best estimates as of July 10, 2001. The projected estimates could change substantially as production and distribution progress. Predictions of monthly vaccine distribution vary by manufacturer, and providers will probably receive the vaccine on different schedules. Because of the 2001-02 influenza season vaccine delay and the large number of doses projected for distribution in November and December, the Advisory Committee on Immunization Practices (ACIP) has developed supplemental recommendations on prioritizing use of the vaccine to ensure that persons at greatest risk for severe complications from influenza and their health care providers, receive the vaccine.

3. POLICY: It is VHA policy to publish annual recommendations on the use of the influenza vaccine.

THIS VHA DIRECTIVE EXPIRES AUGUST 31, 2006

4. ACTION

a. VHA Central Office recommends that the immunization program outlined by the Advisory Committee on Immunization Practices (ACIP) and published in Morbidity and Mortality Weekly Report (MMWR), April 20, 2001/ Vol. 50/ No. RR-04; 1-46, be followed by VA health care facilities.

b. Since manufacturer projections of the influenza vaccine for the 2001-2002 influenza season suggest that approximately 65 percent of the doses will be available for delivery by the end of October 2001, and the remaining doses are projected for distribution in November and December 2001. VHA facilities at the local level are to develop an influenza vaccine prioritization plan that is in alignment with ACIP's recommendations as published in MMWR, July 13, 2001/Vol. 50/No. 27; 582-5.

c. Providers need to target vaccine available in September and October to persons at increased risk for influenza complications and to health care workers. The optimal time for vaccinating high-risk persons is October through November. To avoid missed opportunities, vaccines also need to be offered to the high-risk persons when they access medical care in September, if the vaccine is available. Providers need to continue vaccinating patients, especially those at high risk and in other target groups, in December and should continue as long as there is influenza activity and the vaccine is available.

d. All persons receiving influenza vaccinations should receive information about the vaccine and its benefits and risks. VA Form 10-5549, Influenza Vaccine Consent Form, (see Att. B) is to be completed by all employees receiving the influenza vaccine. ***NOTE:*** *These forms are to be locally reproduced.* The forms may be used for patients as a local option, but written, informed consent is not required when the vaccine is administered in the context of a regular "practitioner-patient" relationship.

5. REFERENCES

a. Centers for Disease Control and Prevention (CDC). Prevention and Control of Influenza: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR, April 20, 2001/ Vol. 50/ No. RR-4; 1-47.

b. Centers for Disease Control and Prevention (CDC). Notice to Readers: Delayed Influenza Vaccine Availability for 2001-02 Season and Supplemental Recommendations of the Advisory Committee on the Immunization Practices," MMWR, July 13, 2001, 50(27);582-5.

c. Physicians Desk Reference, 55th Edition. Medical Economics Co., Inc. Product Information Wyeth-Ayerst Laboratories, pp. 3385-3388; 2001.

d. Centers for Disease Control and Prevention (CDC). General Recommendations on Immunization: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR, January 28, 1994/Vol. 43/No. RR-1; 1-38.

6. FOLLOW-UP RESPONSIBILITY: The Chief, Patient Care Services Officer (11) is responsible for the contents of this Directive. Questions relating to the clinical aspects of the influenza immunization program should be referred to the Office of the Program Director for Infectious Diseases, at (513) 475-6398.

7. RECISSION: VHA Directive 2000-038 is rescinded. This Directive expires August 31, 2006.

S/ Frances Murphy, M.D. for
Thomas L. Garthwaite, M.D.
Under Secretary for Health

Attachments

DISTRIBUTION: CO: E-mailed 8/29/2001
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ATTACHMENT A

INFORMATION ABOUT THE INFLUENZA VIRUS VACCINE FOR 2001 - 2002

1. TARGET GROUPS FOR VACCINATION

a. **Persons at High Risk.** Vaccination is recommended for the following groups of persons who are at increased risk for complications from influenza.

(1) Persons aged ≥65 years;

(2) Residents of nursing homes, other chronic-care facilities that house persons of any age who have chronic medical conditions, and residents of domiciliaries;

(3) Adults who have chronic disorders of the pulmonary or cardiovascular systems, including asthma;

(4) Adults who have required regular medical follow-up or hospitalization during the preceding year because of chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobulinopathies, or immunosuppression (including immunosuppression caused by medications or by human immunodeficiency virus (HIV)); and

(5) Women who will be in the second or third trimester of pregnancy during the influenza season.

b. **Persons Aged 50-64 Years**

(1) Vaccination is recommended for persons aged 50-64 years because this group has an increased prevalence of persons with high-risk conditions.

(2) Persons in this age group without high-risk conditions also receive the benefit from the vaccination in the form of decreased rates of influenza illness, decreased work, absenteeism, and decreased need for medical visits and medication, including antibiotics. Further, 50 years is an age when other preventive services begin and when routine assessment of vaccinations and other preventive services has been recommended.

c. **Persons Who Can Transmit Influenza to Those at High-risk**

(1) Physicians, nurses, and other personnel in both hospital and outpatient-care settings, including emergency response workers;

(2) Employees of nursing homes and chronic-care facilities who have contact with patients or residents;

(3) Employees of assisted living and other residences for persons in groups at high-risk;

(4) Persons who provide home care (e.g., visiting nurses and volunteer workers) to persons in groups at high-risk; and

(5) Household members of persons in groups at high-risk.

d. **Vaccination of Specific Populations**

(1) **Pregnant Women**

(a) Influenza-associated excess deaths among pregnant women were documented during the pandemics of 1918-1919 and 1957-1958. Case reports and limited studies suggest that pregnancy can increase the risk for serious medical complications of influenza as a result of increases in heart rate, stroke volume, and oxygen consumption; decreases in lung capacity; and changes in immunologic function. Women who will be beyond the first trimester of pregnancy (greater than 14 weeks' gestation) during the influenza season need to be vaccinated. Pregnant women who have medical conditions that increase their risk for complications from influenza need to be vaccinated before the influenza season, regardless of the stage of pregnancy.

(b) Because currently available influenza vaccine is an inactivated vaccine, experts consider the influenza vaccination safe during any stage of pregnancy. Some experts prefer to administer the influenza vaccine during the second trimester to avoid a coincidental association with spontaneous abortion (common in the first trimester), and because exposures to vaccines traditionally have been avoided during the first trimester.

(2) **Breastfeeding Mothers**

(a) Influenza vaccine does not affect the safety of mothers who are breastfeeding, or their infants.

(2) Breastfeeding does not adversely affect the immune response and is not a contraindication for vaccination.

(3) **Persons Infected with HIV**

(a) Limited information is available regarding the frequency and severity of influenza illness or the benefits of influenza vaccination among persons with HIV infection.

(b) Because influenza can result in serious illness and because influenza vaccination can result in the production of protective antibody titers, vaccination benefits HIV-infected patients, including HIV-infected pregnant women.

(4) **Travelers**

(a) The risk of exposure to influenza during travel depends on the time of year and destination. In the tropics, influenza can occur throughout the year. In the temperate regions of the Southern Hemisphere, the majority of influenza activity occurs during April through September. In temperate climate zones of the Northern and Southern Hemispheres, travelers also can be exposed to influenza during the summer, especially when traveling as part of large organized tourist groups that include persons from areas of the world where influenza viruses are circulating.

(b) Persons at high-risk for complications of influenza who were not vaccinated with the influenza vaccine during the preceding fall or winter need to consider receiving the influenza vaccine before travel if they plan to:

1. Travel to the tropics;

2. Travel with large organized tourist groups at any time of year; or

3. Travel to the Southern Hemisphere during April through September.

(c) No information is available regarding the benefits of revaccinating persons before summer travel who were already vaccinated in the preceding fall. Persons at high-risk who received the previous season's vaccine before travel need to be revaccinated with the current vaccine in the following fall or winter. Persons aged $\geq$ 50 years and others at high-risk might wish to consult with their physicians before embarking on travel during the summer to discuss the symptoms of influenza, the risks of influenza, and the advisability of carrying antiviral medications for either prophylaxis or treatment of influenza.

(5) **General Population**

(a) Physicians need to administer the influenza vaccine to any person who wishes to reduce the likelihood of becoming ill with influenza, depending on vaccine availability.

(b) Persons who provide essential community services need to be considered for vaccination to minimize disruption of essential activities during influenza outbreaks.

(c) Students or other persons in institutional settings (e.g., those who reside in dormitories) need to be encouraged to receive the vaccine in order to minimize the disruption of routine activities during epidemics.

2. PERSONS WHO SHOULD NOT BE VACCINATED

a. Inactivated influenza vaccine should not be administered to persons known to have anaphylactic hypersensitivity to eggs or to other components of the influenza vaccine without first consulting a physician (see par. 5, Side Effects and Adverse Reactions). Prophylactic use of

the antiviral agents is an option for preventing influenza among such persons. However, persons who have a history of anaphylactic hypersensitivity to vaccine components, but who are also at high risk for complications of influenza, can benefit from vaccine after appropriate allergy evaluation and desensitization. ***NOTE:*** *Information about vaccine components can be found in package inserts from each manufacturer.*

b. Persons with acute febrile illness usually should not be vaccinated until their symptoms have abated. However, minor illnesses with or without fever do not contraindicate the use of influenza vaccine.

3. TIMING FOR ANNUAL VACCINATION

a. The optimal time to vaccinate persons in high-risk groups is usually during October through November. To avoid missed opportunities for vaccination, the influenza vaccine needs to be offered to persons at high-risk when they are seen by health care providers for routine care or are hospitalized in September, provided that vaccine is available. Health care providers need to offer the vaccine to unvaccinated persons after November and throughout the influenza season even after influenza activity has been documented in the community. In the United Sates, seasonal influenza activity can begin to increase as early as November or December but has not reached peak levels in the majority of recent seasons until late December through early March. Therefore, although the timing of influenza activity can vary by region, vaccine administered after November is likely to be beneficial in most influenza seasons. Adults develop peak antibody protection against influenza infection 2 weeks after vaccination.

b. VA facilities planning vaccination campaigns might consider scheduling these events after mid-October. Although influenza vaccine generally becomes available in September, the availability of vaccine in any location cannot be ensured consistently in the early fall. Scheduling campaigns after mid-October will minimize the need for cancellation because the vaccine is unavailable.

c. In facilities housing elderly persons (e.g., nursing homes), vaccination before October generally should be avoided, because antibody levels in such individuals can begin to decline within a few months after vaccination. All residents within a nursing home need to be vaccinated at one time, preceding the influenza season. Residents admitted during the winter months after completion of the vaccination program need to be vaccinated at the time of admission.

4. VACCINE DOSAGE. Adult patients need to receive one intramuscular dose in the deltoid muscle of 0.50 mL of whole (no whole vaccine will be distributed in the United States during the 2001-2002 influenza season) or split-virus containing 15 mg each of A/Moscow/10/99 (H3N2)-like, A/New Caledonia/20/99 (H1N1)-like, and B/Sichuan/379/99-like antigens.

5. SIDE EFFECTS AND ADVERSE REACTIONS

a. Inactivated influenza vaccine contains noninfectious killed viruses and cannot cause influenza. Coincidental respiratory disease unrelated to influenza vaccination can occur after vaccination.

b. **Local Reactions**

(1) The most frequent side effect of the vaccination is soreness at the vaccination site that lasts less than 2 days.

(2) These local reactions generally are mild and rarely interfere with the person's ability to conduct usual daily activities.

c. **Systemic Reactions**

(1) Fever, malaise, myalgia, and other systemic symptoms can occur following vaccination and most often affect persons who have had no exposure to the influenza virus antigens in the vaccine (e.g., young children). These reactions begin 6-12 hours after vaccination and can persist for 1-2 days.

(2) Immediate presumably allergic, reactions (e.g., hives, angioedema, allergic asthma, and systemic anaphylaxis) rarely occur after the influenza vaccination. These reactions probably result from hypersensitivity to some vaccine component; most reactions are likely caused by residual egg protein. Although current influenza vaccines contain only a small quantity of egg protein, this protein can induce immediate hypersensitivity reactions among persons who have severe egg allergy. Persons who have developed hives, have had swelling of the lips or tongue or have experienced acute respiratory distress or collapse after eating eggs need to consult a physician for appropriate evaluation in order to determine if the vaccine needs to be administered. Persons with documented immunoglobulin E (IgE)-mediated hypersensitivity to eggs, including those who have had occupational asthma or other allergic responses to egg protein, might also be at increased risk for allergic reactions to influenza vaccine; therefore, consultation with a physician is to be considered.

(3) Hypersensitivity reactions to any vaccine component can occur. Although exposure to vaccines containing thimerosal can lead to induction of hypersensitivity, most patients do not develop reactions to thimerosal when it is administered as a component of vaccines, even when patch or intradermal tests for thimerosal indicate hypersensitivity. When reported, hypersensitivity to thimerosal usually has consisted of local, delayed-type hypersensitivity reactions.

d. **Guillain-Barre' Syndrome**

(1) Although the 1976 swine influenza vaccine was associated with an increased frequency of Guillain-Barre′ syndrome (GBS), evidence for a casual relationship of GBS with subsequent vaccines prepared from other influenza viruses is unclear. Obtaining strong epidemiologic evidence for a possible small increase in risk is difficult for a rare condition as GBS, which has an annual incidence of only 10-20 cases per million adults, and stretches the limits of epidemiologic investigation. During three of four influenza seasons studied from 1977 through 1991, the overall relative risk estimates for GBS after influenza vaccination were slightly elevated, but were not statistically significant in any of the studies. However, in a study of the 1992-93 and 1993-94 seasons, the overall relative risk for GBS was 1.7 (95 percent confidence interval = 1.0-2.8; p=0.04) during the 6 weeks after vaccination, representing approximately one additional case of GBS per million persons vaccinated. The combined number of GBS cases peaked 2 weeks after vaccination. Thus, investigations to date indicate no substantial increase in GBS associated with influenza vaccines (other than the swine influenza vaccine in 1976) and that, if the influenza vaccine does pose a risk, it is probably slightly more than one additional case per million persons vaccinated.

(2) Even if GBS were a true side effect of vaccination in the years after 1976, the estimated risk for GBS, of approximately one additional case per million persons vaccinated, is substantially less than the risk for severe influenza, which could be prevented by vaccination among all age groups, especially persons aged ≥65 years, and those who have medical indications for the influenza vaccination. The potential benefits of the influenza vaccination in preventing serious illness, hospitalization, and death greatly outweigh the possible risks for developing vaccine-associated GBS. The average case-fatality ratio for GBS is 6 percent, and increases with age. However, no evidence indicates that the case-fatality ratio for GBS differs among vaccinated persons and those not vaccinated.

(3) Whereas the incidence of GBS in the general population is very low, persons with a history of GBS have a substantially greater likelihood of subsequently developing GBS than persons without such a history. Thus, the likelihood of coincidentally developing GBS after the influenza vaccination is expected to be greater among persons with a history of GBS than among persons with no history of this syndrome. Whether the influenza vaccination specifically might increase the risk for recurrence of GBS is not known; therefore, it would seem prudent to avoid the influenza vaccination of persons who are not at high-risk for severe influenza complications and who are known to have developed GBS within 6 weeks of a previous influenza vaccination. Although data are limited, for most persons who have a history of GBS and who are at high risk for severe complications from influenza, the established benefits of the influenza vaccination justify yearly vaccination.

e. Hypoprothombinemia in patients receiving warfarin and elevated theophylline serum concentrations has occurred. Most studies have failed to show any adverse effects of the influenza vaccine in patients receiving these drugs. Nevertheless, monitoring for possible enhanced drug effect or toxicity is indicated for those persons taking theophylline preparations or warfarin sodium.

6. SIMULTANEOUS ADMINISTRATION OF OTHER VACCINES. The target groups for the influenza and pneumococcal vaccination overlap considerably. For persons at high-risk who have not previously been vaccinated with pneumococcal vaccine, health care providers need to strongly consider administering pneumococcal and influenza vaccines concurrently. Both vaccines can be administered at the same time at different sites without increasing side effects. However, the influenza vaccine is administered each year, whereas pneumococcal vaccine is not.

7. ANTIVIRAL AGENTS FOR INFLUENZA

a. Antiviral drugs for influenza are an important adjunct to the influenza vaccine for the control and prevention of influenza. However, they are not a substitute for vaccination. Four currently licensed influenza antiviral agents are available in the United States: amantadine, rimantadine, zanamivir, and oseltamivir.

b. Amantadine and rimantadine are chemically related antiviral drugs with activity against influenza A viruses, but not influenza B viruses. Amantadine was approved in 1966 for prophylaxis of influenza A (H2N2) infection and was later approved in 1976 for the treatment and prophylaxis of influenza type A virus infections in adults and children aged $\geq$1 year. Rimantadine was approved in 1993 for treatment and prophylaxis of infection among adults and prophylaxis among children.

c. Zanamivir and oseltamivir are neuraminidase inhibitors with activity against both influenza A and B viruses. Both zanamivir and oseltamivir were approved in 1999 for the treatment of uncomplicated influenza infections. Zanamivir is approved for treatment for persons aged $\geq$7 years, and oseltamivir is approved for treatment for persons aged $\geq$1 year. In 2000, oseltamivir was approved for prophylaxis of persons aged $\geq$ 13 years.

d. The four drugs differ in terms of their pharmacokinetics, side effects, and costs. ***NOTE:*** *Consult the package inserts for more information.*

8. DEPARTMENT OF VETERANS AFFAIRS (VA) MEDICAL CENTER EMPLOYEES

a. In recent years, many VA medical centers have offered the vaccine (free of charge) because employees may transmit influenza to patients. The influenza vaccine needs to be offered to employees through the Employee Health Program for the purpose of protecting patients served by VA.

b. Immunization records are to be maintained in the Employee Health Unit.

c. Expenses involved in this program need to be kept at a minimum, and for this reason, the use of centrally-procured vaccine vials is recommended instead of unit dose vaccine.

ATTACHMENT B

VA FORM 10-5549, INFLUENZA VACCINE CONSENT FORM

1. The Disease. Influenza (flu) is caused by viruses. When people get flu they may have fever, chills, headache, dry cough or muscle aches. Illness may last several days or a week or more, and complete recovery is usual. However, complications may lead to pneumonia or death in some people. For the elderly and people with diabetes or heart, lung, or kidney diseases, flu may be especially serious.

2. The Vaccine. Today's flu vaccines cause fewer side effects than those used in the past. In contrast with some other vaccines, flu vaccine can be taken safely during pregnancy; however, flu vaccine should be given to pregnant women according to the chronic illness criteria applied to other persons. One shot will protect most people from influenza during the next flu season.

3. Possible Vaccine Side Effects. Most people will have no side effects from the vaccine. However, tenderness at the site of the shot may occur and last for several days. Some people will also have fever, chills, headache, or muscle aches within the first 48 hours.

4. Special Precautions. As with any vaccine or drug, the possibility of severe or potentially fatal reactions exists. However, flu vaccine has rarely been associated with severe or fatal reactions. An uncommon illness characterized by ascending paralysis (Guillain-Barre′ Syndrome) has been reported following other flu vaccines but not in association with this flu vaccine; however, it must be assumed that the risk is present. Hypersensitivity reactions to any vaccine component can occur. Exposure to vaccines containing thimerosal can lead to induction of hypersensitivity. When reported, hypersensitivity to thimerosal has usually consisted of local, delayed-type hypersensitivity reactions (localized swelling and redness). In some instances people receiving vaccine have had allergic reactions. The following precautions should be carefully noted:

a. People with known allergy to eggs should receive the vaccine only for specific indications and under special medical supervision.
b. People with fever should delay getting vaccinated until the fever is gone.
c. People who have received another type of vaccine in the past 14 days should consult a physician before taking the flu vaccine.

NOTE: Please ask if you have any questions about flu or flu vaccine.

I have read the above statement about influenza (flu), the vaccine, and the special precautions. I have had an opportunity to ask questions, and understand the benefits and risks of flu vaccination. I request that it be given to me or to the person named below of whom I am the parent or guardian.

_____ _____
(Print Name of Person to Receive Vaccine) (Date Vaccinated)

_____ _____
(Signature of Person Receiving Vaccine or Parent or Guardian) (Manufacturer & Lot No.)

_____
(Date Signed)

VA Form 10-5549 **REPRODUCE LOCALLY**
Aug 1998